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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/413,110	10/06/99	UNGER	E UNGR-1580

DAVID A CHERRY ESQ
WOODCOCK WASHBURN KURTZ
MACKIEWICZ & NORRIS LLP
ONE LIBERTY PLACE 46TH FLOOR
PHILADELPHIA PA 19103

HM22/1107

EXAMINER

SHARAREH, S

ART UNIT

PAPER NUMBER

1619

DATE MAILED:

11/07/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.
09/413,110

Applicant(s)
Evan Unger

Examiner
Shahnam Sharareh

Group Art Unit
1619



☒ Responsive to communication(s) filed on Aug 21, 2000

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 35 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) 63-67 and 75-115 is/are pending in the application

Of the above, claim(s) 88-93 and 98-107 is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 63-67, 75-87, 94-97, and 108-115 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 9, 10

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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DETAILED ACTION

The Amendment filed on August 21, 2000 has been entered. Accordingly, claim 63 is amended. Claims 63-67, and 75-115 are now pending. Claims 88-93, 98-107 stand withdrawn.

1. Applicant's request in respect to the elected species is considered. Accordingly, upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. Nevertheless, claims 88-93, 98-107 still stand withdrawn.

2. Applicant has not traversed the priority ruling set forth in Paper No. 7, filed on June 6, 2000. Thus, the effective priority date used for the examination of the instant application is October 6, 1999.

Response to Arguments

Claim Rejections - 35 USC § 102

3. Applicant's arguments in respect to the rejection made under 35 U.S.C. 102(b) as being anticipated by Porter et al (Am Heart J 1996 Nov; 132(5):964-968 (abstract)) have been fully considered and are found persuasive in view of the amendment made to claim 63, because Porter does not teach ultrasonic energy being applied via an intravascular or endoluminal ultrasound catheter. Said rejection is withdrawn.

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Claim Rejections - 35 USC § 103

4. Applicant's arguments in respect to the rejection made under 35 U.S.C. 103(a) as being unpatentable over Porter TR et al (Am Heart J 1996 Nov 132(5):964-968 abstract.) ("Am Heart") in view of Porter US Patent 5,648,098 ("098"), and further in view of Schutt et al US Patent 5,626,833 ("833) have been fully considered and are not found persuasive. Claims 63-67, 75-87, 94-97, 108-115 stand rejected.

Applicant argues that none of the cited art teach the intravascular irradiation of ultrasonic energy for lysing of a thrombus, as recited in the amended claims. In response, Examiner states that first, Porter in '098 specifically teach that any ultrasound device can be used to in his method to provide the ultrasonic energy, *col 8 lines 9-11*. Second, Porter et al in Am Heart show that direct application of ultrasonic energy on a clot in combination with a thrombolytic agent enhance clot lysis. Thus, Porter's teachings in combination provide the broad suggestion to an ordinary artisan that direct application of an ultrasonic energy is as effective as transcutaneous application of ultrasonic source. Therefore, it is evident that one can enhance lysis of thrombus when applying ultrasonic energy intravascularly or transcutaneously in combination with a thrombolytic agent, thus although the term intravascular or endoluminal ultrasonic energy is not indicated in either of Porter's teachings, it would have been well within scope of an ordinary skill in the art to determine various possibilities of providing an ultrasonic energy directed to a vascular thrombus.

Finally, Applicant's assertion that Schutt's composition can only be used to enhance visualization of changes in myocardial tissue is considered, nevertheless, Schutt's teachings still

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provide that thrombolytic agents such as TPA or streptokinase can be simultaneously administered with perfluorinated liposomal contrast agents, thus, one of ordinary skill in the art would have been motivated to combine Schutt's suggestion with the methods of Porter to not only improve the lysis of thrombus, but also enhance the visualization, and hence, effectively monitor the clinical efficacy of Porter's method.

New Grounds of Rejection

5. Claim 63-67, 75-87, 94-97, 108-115 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. It appears that the recitation of "ultrasonic energy is applied via an intravascular or endoluminal ultrasound catheter" has no support in the originally filed specification, and thus, it constitutes new matter.

6. Claims 63, 66-67, 75-78, 94-96 rejected under 35 U.S.C. 102(b) as being anticipated by Siegel US Patent 5,9695,460.

The instant claims are now directed to methods of lysing a thrombus comprising (I) administering a thrombolytic agent to a patient, (ii) administering a vesicle composition comprising an aqueous carrier, a gas or gaseous precursor, and vesicles comprising lipids, proteins or polymers to the patient (iii) and applying ultrasonic energy to the thrombus area, wherein the gas comprise a perfluorocarbon, and the thrombus is in a cardiac blood vessel, and wherein said ultrasonic energy is applied via an intravascular or endoluminal ultrasound catheter.

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Siegel et al disclose methods of utilizing a combination of ultrasonic energy and an ultrasonic contrast agent containing perfluorinated microbubbles, *abstract, col 2 lines 1-65, examples 1-5*. Siegel specifically disclose that the ultrasound may be applied intravascularly by means of a miniature ultrasonic transducer or by a guide wire for transmitting ultrasound directly into the vessel, *col 2 lines 7-10*. Siegel's preferred ultrasound contrast agent is Echogen which contains phospholipids therein, *col 5 lines 50-53*. Siegel et al further indicate the use of other types of contrast agents such as gas filled liposomes, or gas filled microbubble for their thrombus lysing method, *col 5 lines 30-48*. Accordingly, Siegel et al meet the limitations set forth in the instant claims.

7. Claims 63-67, 75-87, 94-97, 108-115 rejected under 35 U.S.C. 103(a) as being unpatentable over Siegel et al US Patent 5,695,460 ("460").

The teachings of Siegel et al is described above.

Although Siegel et al do not specifically teach various infusion rates or various types of liposomal entities as the instant claimed invention, he does indicate the use of various types of contrast agents such as gaseous liposomes in this methods, accordingly, it would have been obvious to one of ordinary skill in the art to use a perfluorinated liposomal entity known in the art and further determine its suitable rate of infusion by routine experimentation, because he would have had a reasonable expectation to succeed in enhancing the lysis of a vessel thrombus when utilizing a gas filled liposomal contrast agents. Moreover, changes in rate of administration will not support the patentability of subject matter encompassed by the prior art unless there is

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evidence indicating such rate of administration is critical. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.

8. Claims 63-67, 75-87, 94-97, 108-115 rejected under 35 U.S.C. 103(a) as being unpatentable over Porter US Patent 5,648,098 ("098") in view of Siegel et al US Patent 5,695,460 ("460") and further in view of Schutt et al US Patent 5,626,833 ("833").

The teachings of Porter, Siegel and Schutt are previously described. Porter, Siegel and Schutt are viewed as being in the same field of endeavor because they all teach the enhancement of thrombolytic activity when administering perfluorinated microbubbles.

Although Porter does not teach an intravascular or endoluminal source of ultrasonic energy, one ordinary skilled in the art would have been motivated at the time of invention to use an intravascular or endoluminal source of ultrasonic energy as taught by Siegel, because Porter indicates that any source of ultrasonic energy can be used to lyse a vascular thrombus, and thus an ordinary practitioner would have had a reasonable expectation to succeed in enhancing the lytic effects of thrombolytics of Porter in treating vascular thrombosis when applying an intravascular or endoluminal source of ultrasonic energy. Further, it is well within purview of an ordinary skilled artisan to optimize and determine the suitable rates for administration of the contrast agents that are disclosed by Porter or Siegel. In addition, modifying Porter and Siegel's method in the manner that a gaseous liposome is used as a contrast agent would have also been obvious at the time of invention, because both Porter and Siegel teach methods of using gas filled

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microbubble, wherein the microbubble may be of any available product entity including gas filled liposomes.

Conclusion

9. No claims are allowed. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action, because the scope of the claims has been modified in the manner to require a new search. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh, PharmD whose telephone number is (703) 306-5400. The examiner can normally be reached on Monday to Friday from 8:30 a.m. to 5:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Diana

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Dudash can be reached on 703-308-2328. The fax phone number for this Group is 703-308-4556. Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is 703-308-1235.

sjjs 10/30/00



**DIANA DUDASH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600**
